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Document Title	LETTER FROM INT ISOCYANATE TO USEPA REGARDING TOLUENE DIISOCYANATE
Chemical Category	TOLUENE DIISOCYANATE

2 pgs

INTERNATIONAL ISOCYANATE INSTITUTE, INC.
115 CHERRY HILL ROAD
PARSIPPANY, NEW JERSEY 07054

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5 July 1988

Document Processing Center (TS-790)
Office of Toxic Substances
Environmental Protection Agency
401 M St., SW
Washington, D.C. 20460

ATTN: 8 (e) Coordinator

Dear Sir/Madam:

The International Isocyanate Institute, Inc. (III) is a non-profit corporation organized under the laws of the state of New York. Our members consist of companies engaged in the manufacture of toluene diisocyanate (TDI) and/or diphenyl methylene diisocyanate (MDI) in the Americas, Europe and the Far East. III was formed in 1972 to promote and further the interests of the public, the users and the manufacturers of TDI and MDI in the safe use of these diisocyanates.

The III initiated a two year study of polymeric methylene diphenyl diisocyanate (MDI) at CIVO Institutes, Zeist, The Netherlands, in June 1985. Preliminary results from this study are now available and are now being submitted under section 8 (e) of TSCA.

Male and female rats (Cpb:WU, Wistar Random), 60/sex/level, were exposed for 6 hours/day, 5 days/week for two years to an atmosphere of respirable polymeric MDI (CAS No. 9016-87-9) aerosol. Aerosol concentrations for this study were 0, 0.2, 1.0, and 6 mg/m^3 and were selected based on subchronic studies. An interim sacrifice of a satellite group of 10 additional rats/sex/level was performed at week 52. Animals under study were evaluated using clinical chemistry, hematological, urine analysis, gross and histopathologic procedures.

Due to its physical characteristics, it was not possible to generate a vapor atmosphere of MDI high enough to carry out a meaningful study. Therefore, an aerosol atmosphere was used. The aerosol atmosphere consisted of particles of which 95% were less than 5 µm in diameter. Polymeric MDI was chosen as the test substance as it is the most widely used MDI-based product.

In preliminary studies in rats, the toxicity of MDI was confined to the respiratory tract where it caused irritation at levels of 4 mg/m^3 and above.

In the animals killed after one year of exposure, those exposed to 6 mg/m^3 showed signs of irritation in the nose and lungs and some accumulation of a yellow material in the lungs. At 1 mg/m^3 there were some indications of minor irritation. No effects were observed at 0.2 mg/m^3.

Examination of the rats killed after 2 years of exposure showed that the irritation of the nose and lungs and the accumulation of the yellow material in the lungs continued in the rats exposed to 6 mg/m^3. In the rats exposed to 1 mg/m^3, similar, but lesser, changes were observed. Again, no effects were seen at 0.2 mg/m^3.

The overall tumor incidence, the incidence of malignant tumors, the incidence of benign tumors and the number of tumor-bearing animals did not show differences between the high exposure group and control group. However, when considering individual organs, there was a statistically significant increase in a benign tumor of the lung (adenoma) in 6 of the 60 male rats exposed to 6 mg/m^3. Four of 59 female rats exposed to 6 mg/m^3 and 1 of 60 female rats exposed to 1 mg/m^3 also had a similar benign tumor in their lungs, but neither was statistically significant. In addition, 1 of the 60 male rats exposed to 6 mg/m^3 showed a malignant tumor in its lungs (adenocarcinoma). The presence of a variety of non-neoplastic changes in the lungs, including accumulation of yellow material, indicates the tumors occurred concurrently with irritation of the lungs.

The International Isocyanate Institute is informing its member companies of these findings. The information reported herein is preliminary, and a complete final report of the study will be submitted to the Document Processing Center when it becomes available.

Very truly yours,

Robert K. Rigger
Managing Director

lkr

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Document Title	STATUS REPORT ON POLYMERIC DIPHENYL METHYLENE DIISOCYANATE WITH ATTACHMENTS
Chemical Category	DIPHENYL METHYLENE DIISOCYANATE

PUBLIC FILE COPY

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUL 21 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

CERTIFIED MAIL

Mr. R. K. Rigger
Managing Director
International Isocyanate Institute, Inc.
119 Cherry Hill Road
Parsippany, NJ 07054

Dear Sir:

With regard to:

Section 8(e) notice on: Polymeric Diphenyl Methylene Diisocyanate

Submitted by: International Isocyanate Institute, Inc. (III)

Date submitted: July 5, 1988

EPA Document Control Number: 8EHQ-0788-0741

The Office of Toxic Substances (OTS) has completed a preliminary evaluation of the above referenced submission under Section 8(e), the "substantial risk" information reporting provision of the Toxic Substances Control Act (TSCA). The enclosed status report is the result of that preliminary OTS evaluation but does not necessarily represent EPA's conclusion on polymeric diphenyl methylene diisocyanate (MDI).

With regard to the above referenced TSCA Section 8(e) submission, please ensure that EPA is apprised about all further significant findings from the two-year inhalation study of polymeric MDI that was cited in the submission.

In responding to this request for information, or in otherwise communicating with EPA regarding this submission under Section 8(e), please refer to the EPA Document Control Number that has been assigned to the submission. As in the case of initial 8(e) submissions, all responses/correspondence will be placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA Section 8(e) policy statement ("Statement of Interpretation and Enforcement Policy; Notification of Substantial Risk" 43 FR 11110; March 16, 1978). Any confidentiality claims should be supported by submission of information as described in the enclosed item entitled "Support Information for Confidentiality Claims."

All available information requested by this letter should be transmitted to the EPA Document Processing Center at the address provided below within 20 working days of your receipt of this letter; any requested information or supplemental information that becomes available following your response to this EPA letter should be sent to EPA immediately upon your company's receipt of such information.

Document Processing Center (TS-790)
(Attn: Section 8(e) Coordinator)
Office of Toxic Substances
U.S. Environmental Protection Agency
401 "M" Street, S.W.
Washington, D.C. 20460

Should you have any questions or comments prior to responding to the Agency's request for additional information, please contact Mr. David R. Williams of the Chemical Screening Branch/ECAD at (202)-382-3468.

The Environmental Protection Agency looks forward to continued cooperation with your association and its member companies in the ongoing efforts to evaluate and minimize potential risks posed by chemical substances to health or the environment.

Sincerely,

James F. Darr

James F. Darr, Section Head
Chemical Risk Identification
Section/CSB/ECAD (TS-778)

Enclosures

PUBLIC FILE COPY

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: JUL 15 1988

SUBJECT: Status Report* 8EHQ-0788-0741 Approved: James F. Darr 7/6/88

FROM: David R. Williams, Section 8(e) Coordinator
Chemical Screening Branch/ECAD

TO: James F. Darr, Section Head
Chemical Risk Identification Section/CSB/ECAD

Submission Description

On behalf of its member companies, the International Isocyanate Institute, Inc. (III) provided the following information with regard to the conduct and preliminary findings from a two-year inhalation study of polymeric diphenyl methylene diisocyanate (MDI) in rats being performed for III by the CIVO Institutes, Zeist, The Netherlands:

> "Male and female rats (Cpb:WU, Wistar Random), 60/sex/level, were exposed for 6 hours/day, 5 days/week for two years to an atmosphere of respirable polymeric MDI (CAS No. 9016-87-9) aerosol. Aerosol concentrations for this study were 0, 0.2, 1.0, and 6 mg/m^3 and were selected based on subchronic studies. An interim sacrifice of a satellite group of 10 additional rats/sex/level was performed at week 52. Animals under study were evaluated using clinical chemistry, hematological, urine analysis, gross and histopathologic procedures.
>
> "Due to . . . [the physical characteristics of the test material], it was not possible to generate a vapor atmosphere of MDI high enough to carry out a meaningful study. Therefore, an aerosol atmosphere was used. The aerosol atmosphere consisted of particles of which 95% were less than 5 um in diameter. Polymeric MDI was chosen as the test substance as it is the most widely used MDI-based product.
>
> "In preliminary studies in rats, the toxicity of MDI was confined to the respiratory tract where it caused irritation at levels of 4 mg/m^3 and above.

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* NOTE: This status report is the result of a preliminary evaluation of information submitted to EPA pursuant to Section 8(e), the substantial risk information reporting provision of the Toxic Substances Control Act (TSCA). The statements made in this report should not be regarded as expressing final EPA policy or intent with respect to the subject chemical(s). Any review of this status report should take into account the fact that the report may be based on incomplete information.

"In the animals [that were] killed after one year of exposure, those exposed to 6 mg/m^3 showed signs of irritation in the nose and lungs and some accumulation of a yellow material in the lungs. At 1 mg/m^3, there were some indications of minor irritation. No effects were observed at 0.2 mg/m^3.

"Examination of the rats killed after two years of exposure showed that the irritation of the nose and lungs and the accumulation of the yellow material in the lungs continued in the rats exposed to 6 mg/m^3. In the rats exposed to 1 mg/m^3, similar, but lesser, changes were observed. Again, no effects were seen at 0.2 mg/m^3.

"The overall tumor incidence, the incidence of malignant tumors, the incidence of benign tumors and the number of tumor-bearing animals did not show [any] differences between the high exposure group and control group. However, when considering individual organs, there was a statistically significant increase in benign tumors of the lung (adenoma) in 6 of the 60 male rats exposed to 6 mg/m^3. Four of 59 female rats exposed to 6 mg/m^3 and 1 of 60 female rats exposed to 1 mg/m^3 also had a similar benign tumor in their lungs, but neither was statistically significant. In addition, 1 of 60 male rats exposed to 6 mg/m^3 showed a malignant tumor in its lungs (adenocarcinoma). The presence of a variety of non-neoplastic changes in the lungs, including accumulation of yellow material, indicates the tumors occurred concurrently with irritation of the lungs."

In its Section 8(e) notice, III stated that the association 1) is a non-profit organization comprised of producers of MDI and/or toluene diisocyanate (TDI) "in the Americas, Europe and the Far East," and 2) "was formed in 1972 to promote and further the interests of the public, the users and the manufacturers of TDI and MDI in the safe use of these diisocyanates."

Submission Evaluation

Immediately upon receipt of this TSCA Section 8(e) submission, the Chemical Screening Branch sent a copy of the notice to the Risk Analysis Branch (RAB/ECAD/OTS) for inclusion in the ongoing review of MDI (including polymeric MDI) and other diisocyanates (e.g., TDI). The Chemical Screening Branch will request III to keep EPA apprised of any further significant findings from the two-year inhalation study of polymeric MDI that was cited in the submission.

It should be noted that in 1984, the Chemical Screening Branch prepared "Chemical Hazard Information Profiles" (CHIPs) on MDI (including polymeric MDI) and TDI. These CHIPs contain readily available toxicity and exposure information (as of 1984) on these chemical substances (persons wishing to obtain copies of these CHIPs should contact the TSCA Assistance Office (TAO/OTS) at (202) 554-1404 or write to the TSCA Assistance Office (TS-799), Office of Toxic Substances, U.S. Environmental Protection Agency, 401 "M" Street, S.W., Washington, D.C. 20460). Further, TDI and MDI (including polymeric MDI) are subject of TSCA Section 8(d) and 8(c) information gathering rules. Finally, it should be noted that the Interagency Testing Committee (ITC) has designated hexamethylene diisocyanate (HDI) for testing under Section 4 of TSCA; HDI is also the subject of TSCA Section 8(a) and 8(d) information gathering rules.

Comments/Recommendations

In its Section 8(e) notice, III stated that its member companies were being informed about the reported toxicological findings.

a) The Chemical Screening Branch will request III to ensure that the Agency is apprised about all further significant findings from the two-year inhalation study of polymeric MDI that was cited in III's Section 8(e) submission. The Chemical Screening Branch will forward all reported information to RAB/ECAD for inclusion in the ongoing evaluation of MDI and other diisocyanates.

b) The Chemical Screening Branch will send copies of this status report to NIOSH, OSHA, CPSC, FDA, NTP, OW/EPA, OSWER/EPA, OAR/EPA, ORD/EPA, OPP/EPA, RAB/ECAD/OTS and TRDB/ECAD/OTS; copies of this status report will be sent also to the TSCA Assistance Office (TAO/OTS) for further distribution.

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